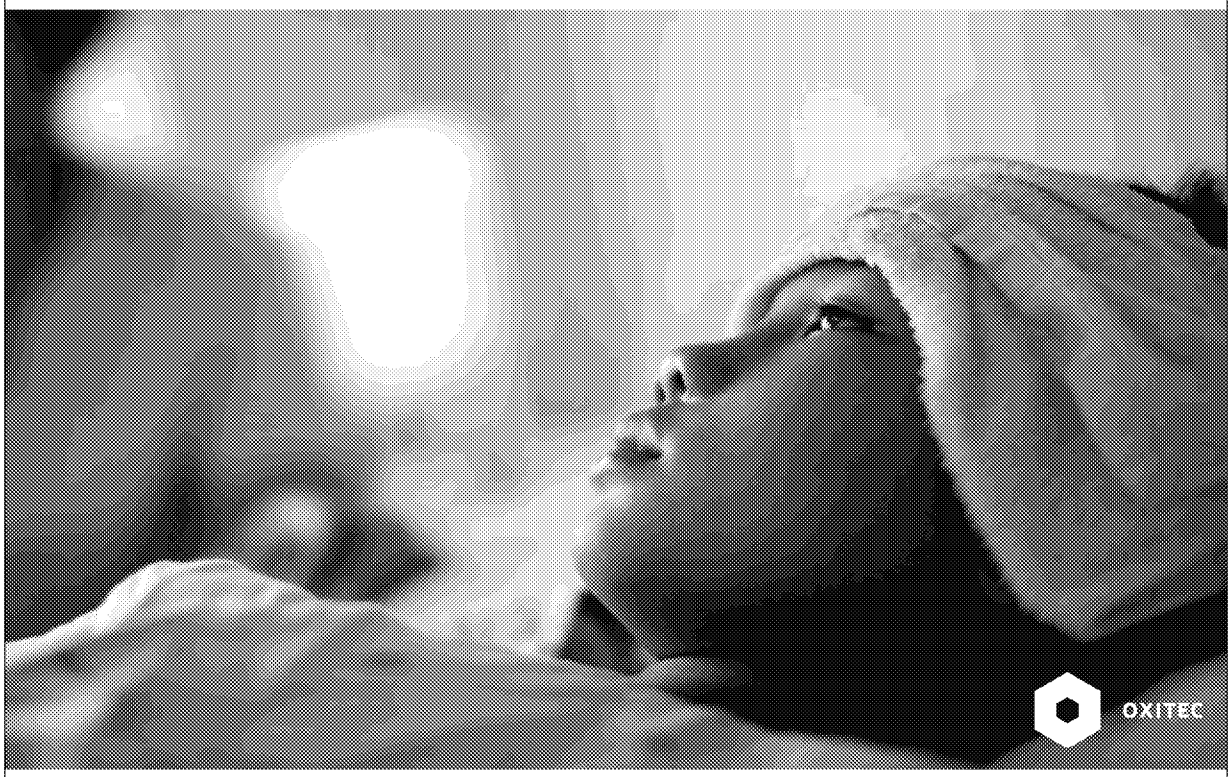
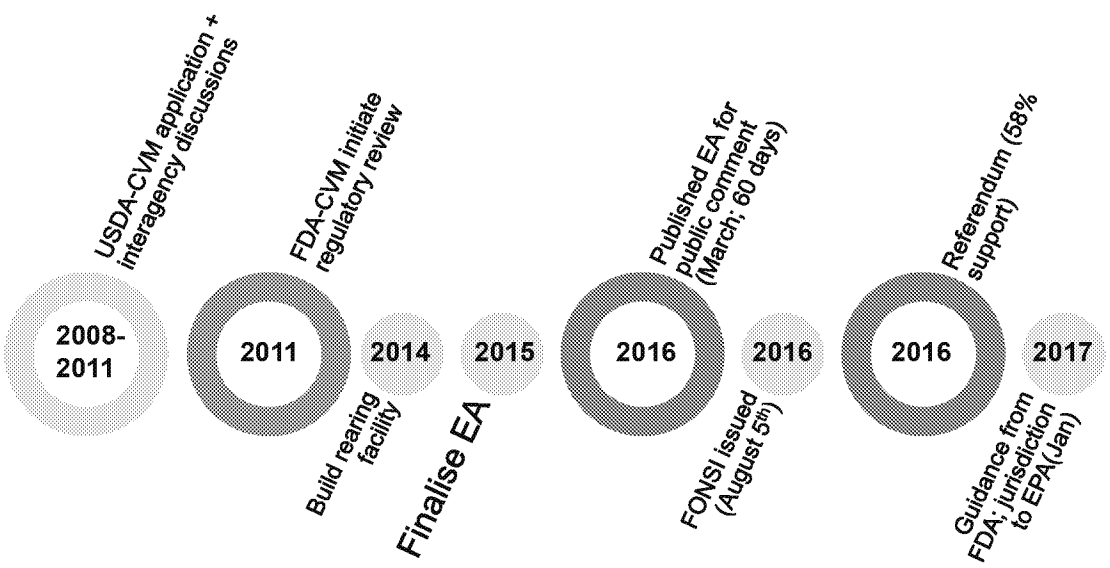
Regulatory Status of OX513A



Regulatory History in the US



Regulatory History (Annotated)

Date	Agency	Outcome
Apr 2008 – Nov 2011	Interagency discussions re for GE mosquito field trial • USDA-APHIS-BRS • EPA • CDC • USDA-APHIS-PPD • USDA-APHIS-VS	Oct 2009 – USDA-VS-NCIE has jurisdiction Mar 2010 – Application for trial submitted to USDA-VS-NCIE NOV 2011 – USDA-VS-NCIE issues letter of no jurisdiction Nov 11 - FDA-CVM has jurisdiction 3 YEARS to determine which agency has jurisdiction
23 Nov 2011	Oxitec opened INAD file 012-109 with FDA	2011 – 2016: requested further information. Achieved concurrence re sections of file (e.g., Molecular characterisation, GE animal lineage, trial protocol)
11 Mar 2016	FDA_CVM post Oxitec's draft EA and FDA's preliminary FONSI for public comment	
5 Aug 2016	FDA – CVM FINAL FONSI Key Haven published	Approx. 5 years to achieve a final FONSI for one trial site
28 Oct 2016	INAD file 012-109 – resubmitted for a new trial site in Monroe County	Amendment submission sent 4 Nov 2016
14 Dec 2016	FDA's letter re incomplete EA	
Jan 2017	FDA_CVM release for comments - Draft Guidance for Industry #236 – Regulation of mosquito related products. Allows jurisdiction transfer to EPA.	Deadline for comments Feb 21 2017
Mar 2017	INAD file 012-109 – re submitted with expanded draft EA for trials and endangered analysis (ESA) resubmitted	
28 Apr 2017	FDA -CVM request further clarifications/ information re trial sites and ESA	

Oxitec Historical Overview

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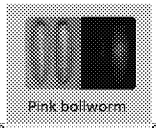
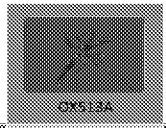

Pink bollworm


OX513A


Brazil facility


OX513A Emerging

2002/4	2005/7	2008/9	2010/12	2013	2014	2015	2016/17
Company formed as spin out from Oxford University Technology platform developed and exemplified in both agricultural and mosquito species  Injection of DNA	Global first release of a GE insect Pink Bollworm (marker only) in USA Mosquito development spurred by Gates funding	First outdoor release of OX513A mosquito in the Caymans Environmental Impact Statement in the USA (GE Pink Bollworm) – environmentally preferred solution World Economic Forum Technology Pioneer 2008 World Economic	First outdoor release of OX513A in Brazil First agricultural collaborations Oxitec Brazil established	Outdoor trials of OX513A in Panama and Brazil First larger scale urban project starts in Jacobina, Brazil First agricultural strains into development Medfly, DBM & Olive fly  Oxitec medfly	Oxitec Brazil National Biosafety approval in Brazil Panama outdoor trial Brazil approval for agricultural trial	First independent projects of OX513A Brazil Oxitec acquired by Intrexon to accelerate development  New UK facility	WHO issues recommendation for OX513A ANVISA announces it will issue RET Grand Cayman launches OX513A FDA publishes final FONSI & EA for Florida Keys Monroe County vote 58% in favour of OX513A Piracicaba expands project & opens new production facility OX513A project begins in India

Step-Wise Evaluation – Field Release

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Cayman	Malaysia	Cayman	Brazil	Brazil	Panama	Brazil	Brazil	Brazil	Cayman
East End	Bentong	East End	Itaberaba	Mandacaru	Nuevo Chorillio	Jacobina	Piracicaba CECAP	Piracicaba CENTRAL	West Bay
2009	2010	2010	2011-12	2012-13	2014	2013-14	2015→	2016→	2016→
1st open release MRR	Open release MRR	>90% control	>90% control	>90% control	>90% control	>90% control	(On-going)	(On-going)	(On-going)
NA	NA	2-300	1,800	2,800	1,000	1,500	5,000	65,000	2 → 50,000

Initial proof of concept, behavioural studies → Operational optimization/use

- Dispersal - > release pattern required
- Longevity - > release interval required
- Monitoring systems
- Dose/release rate required
- Build regulatory dossier

- Release optimization
  - Spatially and temporarily
  - Adaptive release rate
- Monitoring systems optimization
- Mass rearing and Distribution chain
- Data Management System

Regulatory Applications Worldwide

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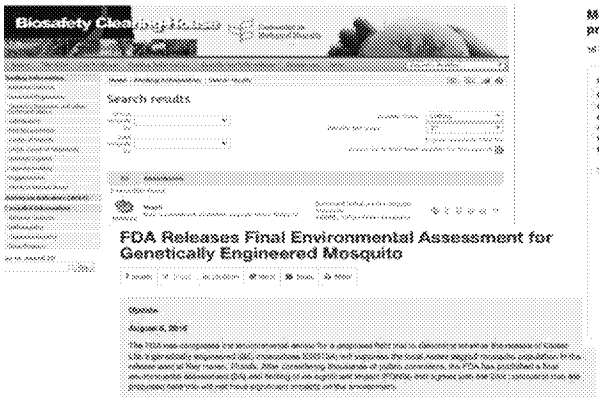
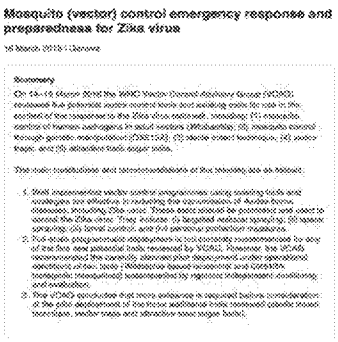
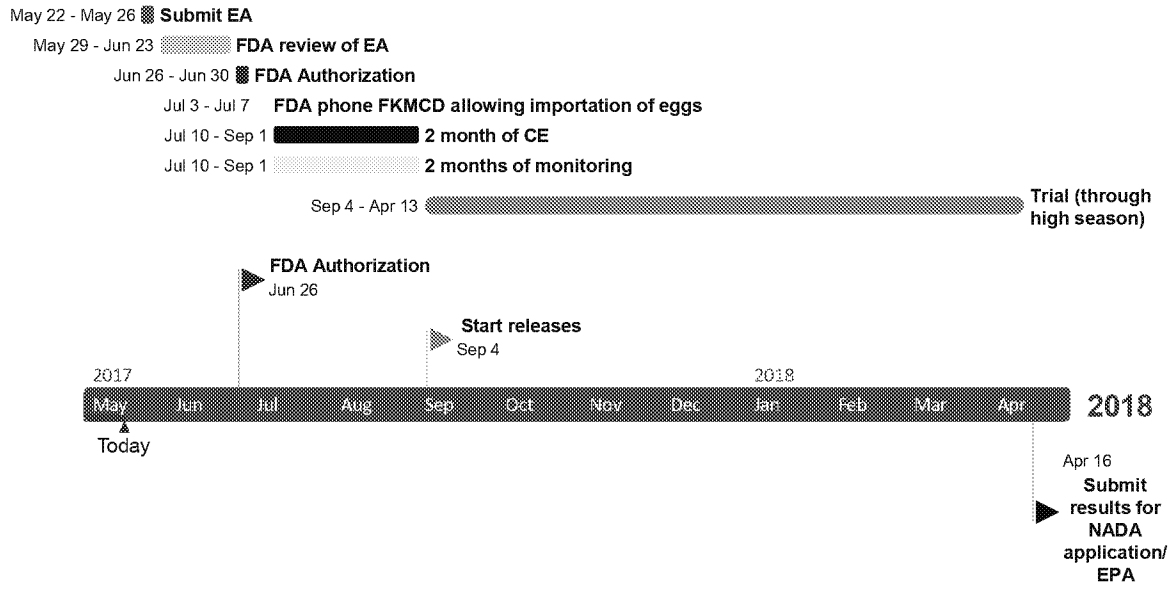
Approvals in Multiple Countries





April 2014	March 2016	April 2016	July 2016	July 2016	August 2016	November 2016
Brazil's CTNBio granted approval for commercial release of Friendly™ *Aedes*	World Health Organization issued recommendation for pilot deployment of Friendly™ *Aedes*	ANVISA announced will issue RET (special temporary registration)	Piracicaba, Brazil, started release of Friendly™ *Aedes* for expansion to cover 60K people	Grand Cayman launched Friendly™*Aedes* to suppress wild *Aedes aegypti*	FDA published final FONSI and environmental assessment for trial in Florida Keys	Florida Keys Mosquito Control District voted to approve trial of Friendly™ *Aedes*

Timeline for Monroe County Trial



Field Trial Timing

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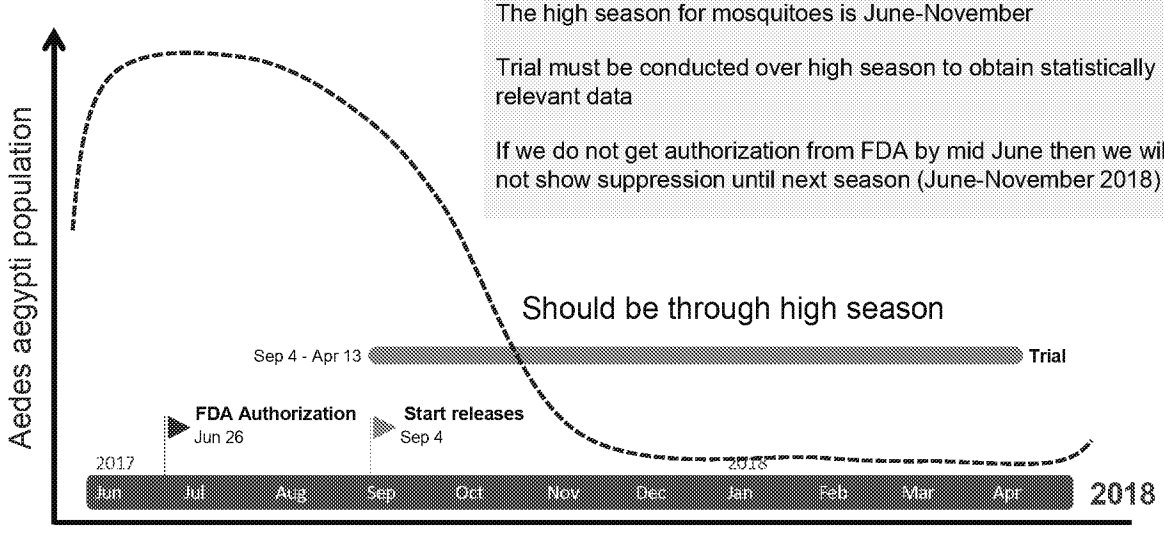
Seasonality of *Aedes aegypti*

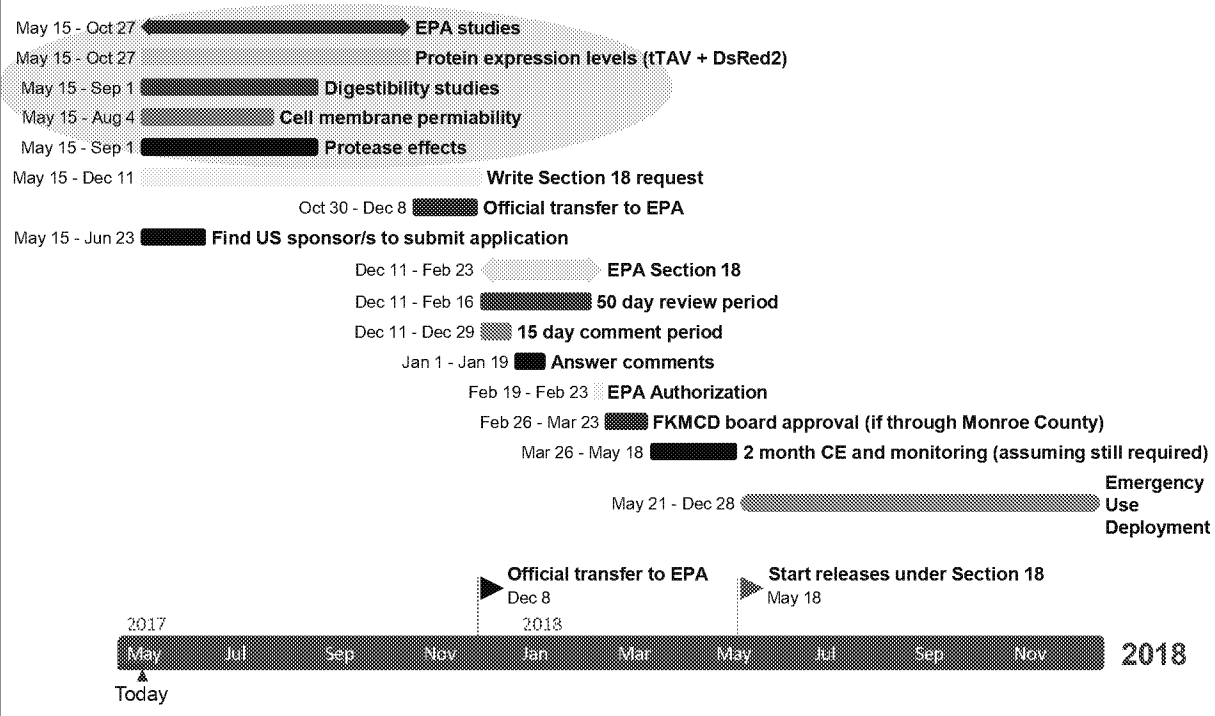
The high season for mosquitoes is June-November

Trial must be conducted over high season to obtain statistically relevant data

If we do not get authorization from FDA by mid June then we will not show suppression until next season (June-November 2018)



Timeline for Section 18 EPA/FDACS



Timeline for Section 18 EPA/FDACS

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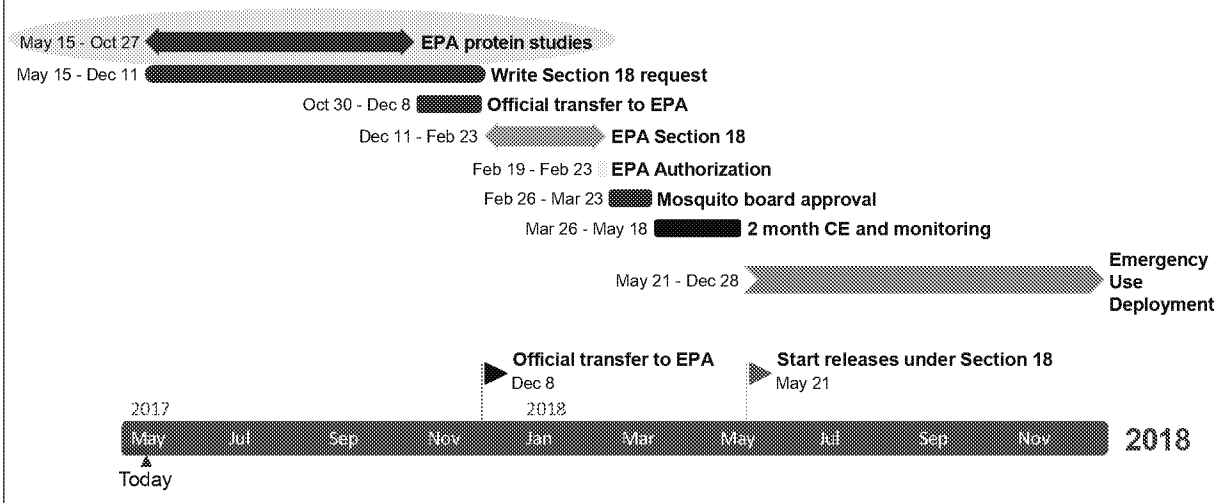
Estimated Timelines for Emergency Use Approval



Timeline EPA EUP Route (Full)

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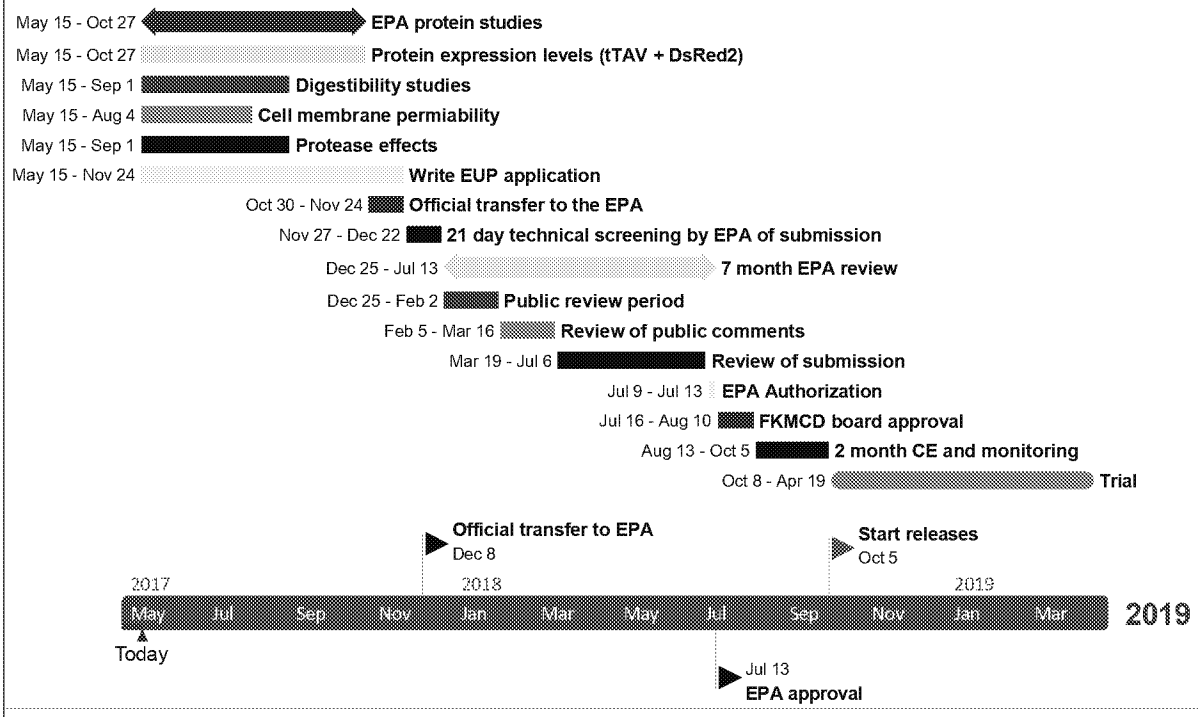

Timeline EPA EUP Route (Full)

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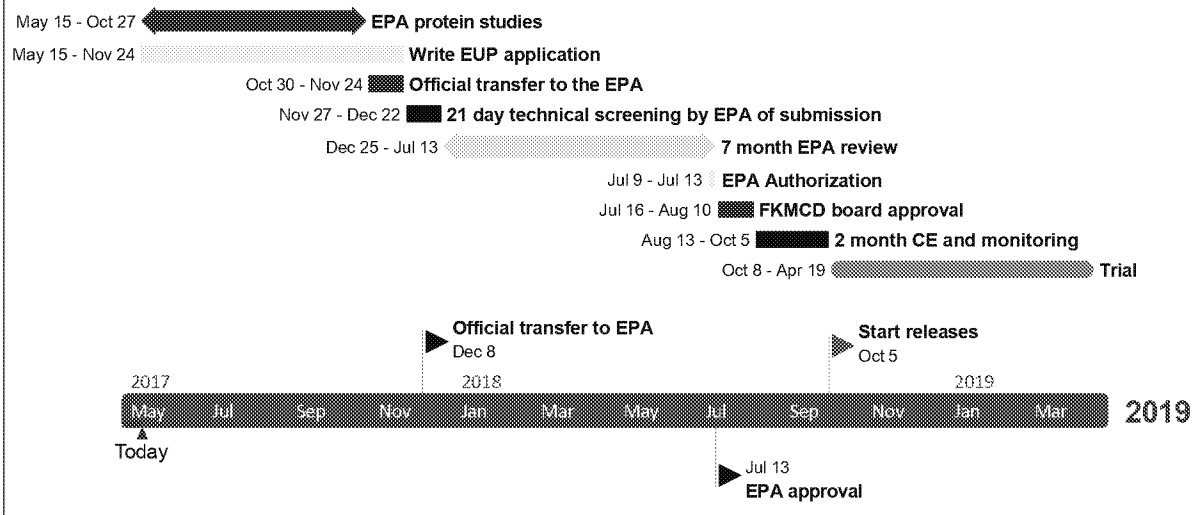
Estimated Timelines for Experimental Use Permit



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Estimated Timeline for Section 3 Registration

Apr 1 - Apr 30 **Complete Monroe County trial**

May 1 **Submit EPA section 3 application**

May 2 - May 23 **21-day Technical Review**

May 24 **Application complete**

May 24 - Jul 24 **Review Application (13 months)**

Jul 26 **EPA Approval**